

# Exhibit C

**UNITED STATES DISTRICT COURT  
DISTRICT OF NEW JERSEY**

MITSUBISHI TANABE PHARMA  
CORPORATION, JANSSEN  
PHARMACEUTICALS, INC., JANSSEN  
PHARMACEUTICA NV, JANSSEN  
RESEARCH AND DEVELOPMENT, LLC,  
and CILAG GMBH INTERNATIONAL,

Plaintiffs,

v.

ZYDUS PHARMACEUTICALS (USA)  
INC.,

Defendant.

**Civil Action No. 17-5005  
(consolidated)**

**Contains Highly Confidential  
Information**

**OPENING EXPERT REPORT OF FABIA GOZZO, PH.D.**

I, Fabia Gozzo, Ph.D., submit the following report on behalf of Mitsubishi Tanabe Pharma Corp., Janssen Pharmaceuticals, Inc., Janssen Pharmaceutica NV, Janssen Research and Development, LLC, and Cilag GmbH International (collectively, “Plaintiffs”) in this action.

## **I. EXPERT QUALIFICATIONS**

### **A. Area of Expertise**

1. Based on my experience and qualifications, I consider myself an expert in X-ray powder diffraction technique, including synchrotron X-ray powder diffraction, and instrumentation for crystal structure phase determination, identification and quantification.

### **B. Educational Background**

2. I obtained my Ph.D. in Physics in 1995 from the Ecole Polytechnique Federale de Lausanne (EPFL), Switzerland. I joined Lawrence Berkeley National Laboratories in Berkeley, California in 1995 as a Postdoctoral Researcher where I worked on the development of x-ray spectromicroscopy for industrial applications.

### **C. Relevant Professional Experience**

3. I am the Founder, Chief Executive Officer, and Managing Director of Excelsus Structural Solutions (ESS hereinafter), with offices in Brussels, Belgium and Villigen, Switzerland. I have over 25 years of experience working in the materials science field.

4. In 1996, after my Postdoctoral Research, I joined Intel Corporation in Santa Clara, California as Research Scientist where I, among other things, worked on the development of x-ray spectromicroscopy for chemical analyses of semiconductor microstructures.

5. After moving back to Europe in 1998, I worked at the Paul Scherrer Institute – Swiss Light Source in Villigen, Switzerland, first as a Project Leader and then as Senior Researcher – Beamline Scientist until 2011. In the latter role, I was responsible for the

construction, development and management of the lab that performed synchrotron X-ray powder diffraction (“S-XRPD”) testing and analysis.

6. In 2012, I founded Excelsus Structural Solutions, which provides synchrotron radiation based analytical services and scientific consulting in the field of structural characterization of materials and quantitative phase analysis. My work involves performing or supervising S-XRPD testing.

7. For further details regarding my experience and qualifications, including publications, a copy of my curriculum vitae is attached as Exhibit 1. During the previous four years, I have not testified as an expert at trial or by deposition in any case.

**D. Compensation**

8. I am compensated at my standard rate of CHF 370/hr. No part of my compensation is contingent upon the outcome of this case or any issue in it, and I do not have any financial interest in any of the companies involved in this lawsuit.

**E. Material Considered**

9. A list of materials that I considered for purposes of this report are attached as Exhibit 2. I also relied on my background knowledge, experience, and training in the relevant scientific areas.

**II. OVERVIEW OF WORK PERFORMED**

10. I was asked by counsel to perform S-XRPD testing on samples of Defendant Zydus Pharmaceuticals (USA), Inc. (“Zydus”) canagliflozin drug products (“Zydus’s ANDA Products”). I performed such testing at the Swiss synchrotron facility Swiss Light Source at the X04SA Materials Science beamline – Powder Diffraction station. I present the results below.

**III. SYNCHROTRON-XRPD**

11. Phase analysis of pharmaceutical compounds with X-ray powder diffraction

("XRPD") is a widely used and established practice in the pharmaceutical industry. XRPD is an analytical technique that uses the interaction between X-rays and matter to study the structural and microstructural properties of a material in the form of a crystalline powder. In an XRPD analysis, often conducted in a conventional laboratory using an X-rays tube as a source of X-rays (so-called laboratory-XRPD) a sample is irradiated with X-rays and the X-rays diffracted by the sample are recorded by a detector. XRPD measures the way in which a crystalline structure diffracts X-rays. That diffraction of X-rays varies based on the arrangement of the molecules within a crystalline molecular structure.

12. Based on the diffraction of the X-rays, XRPD produces a pattern of peaks that are unique to that crystalline form of a powder compound. This pattern of peaks is referred to interchangeably as a powder diffraction pattern, powder diffractogram, or XRPD pattern. The position, intensity, width, and shape of the peaks (so-called Bragg peaks) form the diffraction pattern. Each crystalline form of a compound has its own characteristic or unique XRPD pattern. Based on differences in diffraction patterns, XRPD can distinguish different crystalline forms of a compound. It can therefore be used to detect the presence of a particular crystalline form in a mixture of other solid forms of a compound.

13. Synchrotron X-ray powder diffraction (S-XRPD) is a technique that uses a synchrotron source as a source of X-rays to perform XRPD measurements. A synchrotron is an extremely powerful source of X-rays that are produced by high-energy electrons when their path changes direction due to high intensity magnetic fields. This powerful X-ray beam is maintained at a synchrotron facility.

14. Because of its high beam intensity and high degree of collimation, S-XRPD is capable of detecting the presence of crystalline phases that are present in a mixture in small amounts. Furthermore, S-XRPD readily allows measurements to be performed in transmission mode on intact formulated drugs (e.g. powders, pellets, tablets) without

requiring any special sample treatment prior to the measurements. During an S-XRPD measurement in transmission mode, the powder sample can be loaded in a glass capillary, which is then exposed to the X-rays while the capillary is spun around its axis. Spinning the capillary during the measurement is a common practice in XRPD measurements in transmission because it allows a much larger number of the crystallites composing the powder sample to diffract the X-rays.

#### IV. TESTING OF ZYDUS'S ANDA PRODUCTS

15. I was asked to conduct S-XRPD testing of Zydus's ANDA Products. In the section below, I provide details related to the samples tested and the methods used.

##### A. **Materials and Methods**

##### 1. **Samples Tested**

16. I conducted testing on the following samples of Zydus's ANDA Products:

| ESS ID | Zydus Lot Number | Compound       | Storage conditions |
|--------|------------------|----------------|--------------------|
| QE49   | ME68463          | 100 mg tablets | Controlled ambient |
| QE50   | ME68463          | 100 mg tablets | Controlled ambient |
| QE51   | ME68463          | 100 mg tablets | Controlled ambient |
| QE52   | ME68464          | 100 mg tablets | Controlled ambient |
| QE53   | ME68464          | 100 mg tablets | Controlled ambient |
| QE54   | ME68464          | 100 mg tablets | Controlled ambient |
| QE55   | ME68465          | 100 mg tablets | Controlled ambient |
| QE56   | ME68465          | 100 mg tablets | Controlled ambient |
| QE57   | ME68465          | 100 mg tablets | Controlled ambient |
| QE58   | ME68475          | 300 mg tablets | Controlled ambient |
| QE59   | ME68475          | 300 mg tablets | Controlled ambient |
| QE60   | ME68475          | 300 mg tablets | Controlled ambient |
| QE61   | ME68476          | 300 mg tablets | Controlled ambient |
| QE62   | ME68476          | 300 mg tablets | Controlled ambient |
| QE63   | ME68476          | 300 mg tablets | Controlled ambient |
| QE64   | ME68477          | 300 mg tablets | Controlled ambient |
| QE65   | ME68477          | 300 mg tablets | Controlled ambient |
| QE66   | ME68477          | 300 mg tablets | Controlled ambient |

| ESS ID | Zydus Lot Number | Compound               | Storage conditions |
|--------|------------------|------------------------|--------------------|
| QE67   | ME68500          | 50 mg/500 mg tablets   | Controlled ambient |
| QE68   | ME68502          | 50 mg/500 mg tablets   | Controlled ambient |
| QE69   | ME68504          | 50 mg/500 mg tablets   | Controlled ambient |
| QE70   | ME68506          | 50 mg/1000 mg tablets  | Controlled ambient |
| QE71   | ME68508          | 50 mg/1000 mg tablets  | Controlled ambient |
| QE72   | ME68510          | 50 mg/1000 mg tablets  | Controlled ambient |
| QE73   | ME68512          | 150 mg/500 mg tablets  | Controlled ambient |
| QE74   | ME68514          | 150 mg/500 mg tablets  | Controlled ambient |
| QE75   | ME68516          | 150 mg/1000 mg tablets | Controlled ambient |
| QE76   | ME68520          | 150 mg/1000 mg tablets | Controlled ambient |
| QE77   | ME68523          | 150 mg/1000 mg tablets | Controlled ambient |

17. On August 26, 2019, a parcel containing samples of Zydus's ANDA Products was delivered to Excelsus Structural Solutions (Swiss) AG's premises located at PARK INNOVAARE, CH-5234 Villigen, Switzerland from Karen Gushurst at AMRI SSCI, LLC in West Lafayette, Indiana. (*See Exhibit 3.*)

18. The samples of Zydus's ANDA Products were received in a room temperature shipment packaged in a Ziplock bag containing Drierite desiccant inside a Uline insulated container within a World Courier box. (*See Exhibit 3.*) Upon receipt, the parcel was immediately taken in a laboratory with controlled temperature at  $22 \pm 2$  °C and ambient relative humidity, opened and its contents inspected, photographed, and labeled by ESS Principle Scientist, Dr. Mickael Morin, according to ESS Standard Operating Procedure. (*See Exhibit 4.*) The sample information was then entered into the ESS sample tracking database. After processing the samples, Dr. Morin immediately stored the samples in a temperature controlled locker at  $22 \pm 2$  °C at ambient relative humidity in light protected containers. Each of the samples were labeled with an ESS ID QE number from 49 to 77. (*See Exhibit 5.*)

## 2. Testing of Zydus's ANDA Products Via S-XRPD

### a. Instrumentation and Calibration

19. On November 11, 2019 and November 18, 2019, S-XRPD measurements on Samples QE49 through QE77 were performed. MYTHEN II 1-Dimensional (1-D) solid-state silicon microstrip detector ("MYTHEN II detector") was used set at a discriminator threshold of 6200 eV appropriate for the working synchrotron photon energy of 12.4 keV. MYTHEN II detector is a modular detector. The MYTHEN II detector at the Swiss Light Source at the X04SA Materials Science beamline–Powder Diffraction station covers a total angular range of 120 degrees in  $2\theta$  by assembling 24 modules mounted one next to the other.

20. All S-XRPD measurements were performed using a synchrotron photon wavelength of  $\lambda = 1.0008445(4) \text{ \AA}$  (November 11<sup>th</sup>, 2019 beamtime) and  $\lambda = 1.0008814(9) \text{ \AA}$  (November 18<sup>th</sup>, 2019 beamtime) corresponding to nominal 12.4 keV, as carefully calibrated by Pawley refinement of the silicon powder from the National Institute of Standards and Technology (NIST640D). There is an offset of  $-0.00032(2)^\circ$  of the  $2\theta$  scale (so-called  $2\theta$ -zero-offset) associated with  $\lambda=1.0008445(4) \text{ \AA}$  (November 11<sup>th</sup>, 2019 beamtime) and an offset of  $0.00004(3)^\circ$  of the  $2\theta$  scale (so-called  $2\theta$ -zero-offset) associated with  $\lambda=1.0008814(9) \text{ \AA}$  (November 18<sup>th</sup>, 2019 beamtime)

21. Prior to testing Samples QE49 through QE77, the MYTHEN II detector was carefully calibrated using a standard reference powder of silicon (NIST640D powder) and a reference sample of amorphous silica rod to deliver diffraction patterns with both calibrated angular scale (using silicon NIST640D) and calibrated scattered intensity (using an amorphous silica rod), the latter via so-called "flatfield" calibration files. (*See* Exhibit 6.) Angle and intensity calibration files are subsequently used by a data reprocessing software to generate reprocessed calibrated powder diffraction patterns. This software was developed by scientists at the Swiss Light Source X04SA Materials Science beamline – Powder Diffraction

station. With the refinement of the diffraction pattern of the silicon powder (NIST640D powder), I carefully verified, as is my usual practice, that all calibrations were performed correctly and the diffraction patterns were of the expected quality.

### **b. Sample Preparation**

22. On November 8th, 2019, a tablet of each of QE49 through QE77 samples listed in the Table at paragraph 16 was prepared for S-XRPD testing according to the following protocol:

- Each of the glass bottles containing the QE49 through QE77 tablets was introduced in a freshly cleaned glove box, one at a time. The glass bottle was opened and one tablet extracted. The tablet was first peeled to remove its coating using a clear micro-tweezer, then halved. One half of the tablets was gently grinded to a powder, the second saved in a separate new glass vial. The powder from one half of the tablet was then loaded into 0.8 mm G50 borosilicate Hilgenberg capillaries at ambient conditions of relative humidity and controlled temperature ( $22 \pm 2$  °C ).
- For each sample, a capillary length of minimum 3-4 cm was loaded with the powder from the gently grinded tablet with the help of a spatula and gentle vibrations of the glass capillary. The glove box and tools were carefully cleaned after each sample preparation.
- Once loaded with a sufficient amount of powder (i.e. at least 3-4 cm of the capillary length), the glass capillary was cut with a pincer, sealed with cyanolit glue on the opened side and secured first on a brass button, then on a magnetic attachment ready to be mounted at the center of the diffractometer.
- Temperature and relative humidity were monitored during sample preparation. The temperature and relative humidity were recorded by a monitor placed inside the glove box and were also manually recorded in the *Sample Preparation Check-List* form (see Exhibit 7). The monitoring of these values determined that the environmental conditions were  $22 \pm 2$  °C and  $40 \pm 5\%$  RH.

### **c. Data Collection**

23. To conduct the synchrotron measurements, the glass capillary was placed on a rotation stage (so-called spinner) integrated to an automatic sample alignment system equipped with additional 4 degrees of freedom (2 linear movements, 2 angular movements) to accurately align the capillary at the center of the diffractometer. An additional linear degree of freedom allows one to translate the capillary perpendicular to the X-ray synchrotron beam and, therefore, select a given portion of the powder sample for the analysis. Once carefully

aligned, the glass capillary was spun at 4Hz with a spinner available at the Swiss Light Source powder diffraction beamline, as is common practice in powder diffraction measurements for improved statistics of the powder crystallites orientation. Prior to the measurements, the synchrotron photon beam was focused on the vertical plane (i.e. the diffraction plane) to improve the diffraction peaks' line shape at low  $2\theta$  angles and the angular resolution. A beam-stop, which is a short anti-scatter extension, was placed between the capillary and the detector to block the direct intense synchrotron beam around  $2\theta=0^\circ$ .

24. For each sample, the high-intensity focused synchrotron photon beam of X-rays hit the capillary as it was spun. The Mythen II 1-dimensional detector was positioned at a fixed position of 760 mm away from the sample. The detector measured the X-rays scattered by the sample as the high intensity X-rays passed through the material in the capillary.

25. For each sample of QE49 through QE77, the scattered intensity from the X-rays was collected as a function of the  $2\theta$  scattering angle (referred to as a "full diffraction pattern") from 3 different powder volumes (i.e. cylindrical volumes of 0.8mm diameter and 4mm height) along the glass capillary.

26. For each powder volume, referred to as volume P1, P2 or P3 in the data files, the full diffraction patterns were recorded at eight different detector angular  $2\theta$  positions and in short multiple 5-second full diffraction patterns often referred to as "runs". This acquisition sequence was then repeated three times for each powder volume P1, P2 and P3.

27. After each data collection, I individually inspected each run for radiation damage of the sample. There was no sign of radiation damage in any of the QE49 through QE77 samples.

28. Then, using software developed by the Swiss Light Source powder diffraction beamline scientists (called Postpro\_2014, written in Fortran language), I processed all the

individual 5-second full diffraction patterns to generate merged diffraction patterns (i.e., compilations of the 72 individual 5-seconds powder diffraction patterns). For each sample of QE49 through QE77, the net acquisition time of a merged diffraction pattern was, therefore, 360 seconds (72 x 5 seconds).

29. A measurement of an empty capillary and the air (i.e. without sample and empty capillary) were also recorded under the same experimental conditions described above for samples QE49 through QE77. This was done, as usual, to confirm that neither the capillary nor the air made any contribution to the resulting diffraction patterns.

#### **B. Results**

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

#### **I. SUPPLEMENTATION**

31. I reserve the right to supplement or amend my report in response to opinions expressed by Zydus's experts, or in light of additional evidence, testimony, discovery, or other information that may be provided to me after the date of this report.

32. I also reserve the right to offer additional testimony, if necessary, concerning the subject matter of the patents-in-suit.

33. In addition, I expect that I may be asked to consider and testify about issues that may be raised by Zydus's fact witnesses and technical experts at trial or in their reports.

It may also be necessary for me to supplement my opinions as a result of ongoing discovery, Court rulings and testimony at trial.

## **II. TRIAL EXHIBITS**

34. I may rely on visual aids and demonstrative exhibits that demonstrate the bases for the testing in my report. These visual aids and demonstrative exhibits may include, for example, interrogatory responses, deposition testimony and exhibits, as well as charts, photographs, diagrams, videos, and animated or computer-generated videos.

Executed this 6<sup>th</sup> day of February 2020, I declare under penalty of perjury that the foregoing is true and correct.

A handwritten signature in blue ink, appearing to read "Fabia Gozzo". The signature is written in a cursive, flowing style.

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Fabia Gozzo, Ph.D.